Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method for constructing a variant set for an antibody of interest, the method comprising:

(a) ~~a)~~ identifying, ~~using a plurality of rules,~~ a plurality of positions in said antibody of interest and, for each respective position in said plurality of positions, one or more substitutions for the respective position, wherein the plurality of positions and the one or more substitutions for each respective position in the plurality of positions collectively define an antibody sequence space;

(b) ~~b)~~ selecting a first plurality of variants of the antibody of interest, thereby forming a variant set, wherein said variant set comprises ~~a plurality of variants of said antibody of interest and wherein said variant set is~~ a subset of said antibody sequence space;

(c) ~~c)~~ measuring a property of all or a portion of the variants in said variant set;

(d) ~~d)~~ modeling a sequence-activity relationship between (i) one or more substitutions at one or more positions of the antibody of interest ~~represented by~~ in the variant set and (ii) the property measured for all or said portion of the variants in the variant set, and then deriving from the sequence-activity relationship:

(A) a plurality of first values, wherein each first value in the plurality of first values is the contribution to the measured property by the one or more substitutions at one or more positions in the plurality of positions in the antibody of interest, and

(B) a plurality of second values, wherein each second value in the plurality of second values quantifies a confidence of a first value in the plurality of first values; ~~and~~

(e) ~~e)~~ redefining said variant set to comprise variants in said antibody sequence space that include substitutions in said plurality of positions that are selected based on a function of said ~~sequence-activity relationship~~ plurality of first values and said plurality of second values; and

(f) measuring a property of all or a portion of the variants in said variant set after said variant set has been redefined in step (e).

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2. (Currently amended) The method of claim 1, the method further comprising repeating said measuring step (c), said modeling step (d), and, optionally, said redefining step (e), and said measuring step (f) until a variant in said variant set exhibits a value for said property that exceeds a predetermined value.

3. (Original) The method of claim 2 wherein said predetermined value is a value that is greater than the value for the property that is exhibited by said antibody of interest.

4. (Currently amended) The method of claim 1, the method further comprising repeating said measuring step (c), said modeling step (d), and, optionally, said redefining step (e), and said measuring step (f) until a variant in said variant set exhibits a value for said property that is less than a predetermined value.

5. (Currently amended) The method of claim 1 [[4]], wherein said predetermined value is a value that is less than the value for the property that is exhibited by said antibody of interest plurality of positions and the one or more substitutions for each respective position in the plurality of positions are identified in step (a) using a plurality of rules.

6. (Currently amended) The method of claim 5, 1, the method further comprising repeating said measuring, modeling, and optionally, said redefining, a predetermined number of times wherein each rule in the plurality of rules defines an action to be taken in response to a computational test selected from the group of computational tests consisting of:

    (i) a proximity of a position in the plurality of positions to a structurally defined region within the antibody;

    (ii) a physico-chemical property of an amino acid at a position within a plurality of antibody sequences;

    (iii) a principal component analysis of amino acids found at one or more positions within a plurality of antibody sequences;

    (iv) a presence or an absence of a substitution in an antibody that is homologous to said antibody of interest;

    (v) a presence or an absence of a substitution in a specific class of antibodies that are homologous to said antibody of interest;

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(vi) a favorability of a substitution to a position in the antibody of interest calculated using a substitution matrix;

(vii) a probability of a substitution to a position in the antibody of interest calculated from a conservation index;

(viii) a favorability of a substitution to a position in the antibody of interest calculated from a comparison of homologous sequences;

(ix) a mutability of a position in the antibody of interest calculated from a comparison of homologous sequences;

(x) a favorability of a substitution to a position in the antibody of interest calculated from a comparison of structures that are homologous to said antibody of interest; and

(xi) a mutability of a position in the antibody of interest calculated from a comparison of structures that are homologous to said antibody of interest.

7. (Cancelled)

8. (Currently amended) The method of claim 1, wherein said sequence-activity relationship comprises a plurality of values and wherein each value in said plurality of first values describes a relationship between the property measured in step (c) and:

(i) a substitution at a position in said plurality of positions represented by [[said]] all or said portion of the variants in said variant set and said property,

(ii) a plurality of substitutions at a position in said plurality of positions represented by [[said]] all or said portion of the variants in said variant set and said property, or

(iii) one or more substitutions in one or more positions in said plurality of positions represented by [[said]] all or said portion of the variants in said variant set and said property.

9. (Currently amended) The method of claim 8, wherein said modeling comprises regressing:

$$V_{measured} = W_{11}P_1S_1 + W_{12}P_1S_2 + \ldots + W_{1N}P_1S_N + \ldots + W_{M1}P_MS_1 + W_{M2}P_MS_2 + \ldots + W_{MN}P_MS_N$$

wherein,

$V_{measured}$ [[represents]] is the property measured in variants in step (c) in said variant set;

W_{MN} [[=]] is a value in said plurality of first values;

P_M [[=]] is a position ~~in~~ said ~~antibody of interest~~ in said plurality of positions in said antibody of interest; and

S_N [[=]] is a substitution ~~in the one or more positions for a~~ <u>at a</u> position in the plurality of positions in said antibody of interest.

10. (Original) The method of claim 9, wherein said regressing comprises linear regression, non-linear regression, logistic regression, multivariate data analysis, or partial least squares projection to latent variables.

11. (Currently amended) The method of claim 1<u>,</u> wherein said modeling <u>step (d)</u> comprises computation of a neural network, computation of a ~~bayesian~~ <u>Bayesian</u> model, computation of a generalized additive model, computation of a support vector machine, or classification using a regression tree.

12. (Currently amended) The method of claim 1, wherein said modeling <u>step (d)</u> comprises boosting or adaptive boosting.

13. (Currently amended) The method of claim 1<u>,</u> wherein said redefining <u>step (e)</u> further comprises:

 <u>computing, for each respective first value in the plurality of first values, a modified respective first value by modifying the respective first value based on a function of a second value, in the plurality of second values, that corresponds to the respective first value, thereby computing a plurality of modified first values; and</u>

 computing a predicted score<u>, for each respective variant in</u> [[for]] a population of variants of said antibody of interest<u>,</u> using ~~said sequence-activity relationship~~ <u>the plurality of modified first values, thereby computing a plurality of predictive scores,</u> wherein each variant in said population of variants includes a substitution at one or more positions in said plurality of positions in said antibody of interest; and

 ~~selecting~~ <u>redefining</u> said variant set <u>by selecting variants</u> from among said population of variants as a function of the predicted score received by each variant in said set of variants.

14. (Currently amended) The method of claim 13, the method further comprising<u>:</u>

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ranking said population of variants, wherein each variant in said population of variants is ranked based on the predicted score received by the variant based upon the sequence-activity relationship; and

said selecting comprising accepting a predetermined percentage of the top ranked variants in said population of variants for said variant set.

15. (Cancelled)

16. (Currently amended) The method of claim 1, wherein said redefining step (e) further comprises redefining said variant set to comprise one or more variants of the antibody ~~each having a substitution in a position in said plurality of positions not present in any variant in the variant set selected in said selecting step (b)~~ that are not in the antibody sequence space of step (a).

17-19 (Cancelled)

20. (Currently amended) The method of claim ~~18~~ 1, wherein said redefining step (e) further comprises redefining said variant set to comprise one or more variants each having a substitution in a position in said plurality of positions not present in any variant in the variant set selected by said selecting step (b).

21. (Currently amended) The method of claim ~~1~~ 5, wherein

the contribution of each respective rule in said plurality of rules to the defining of said antibody sequence space is independently weighted by a rule weight in a plurality of rule weights corresponding to the respective rule; and

the method further comprising, prior to said redefining step (e), the steps of:

adjusting one or more rule weights in said plurality of rule weights based on a comparison, for each respective ~~variant~~ substitution at each position in the plurality of positions in the variant set, of (i) a value ~~assigned to~~ derived for the respective ~~variant by said~~ substitution from the sequence-activity relationship, and (ii) a score assigned by the plurality of rules to the respective ~~variant~~ substitution; and

repeating said identifying step using said rule weights, thereby redefining said plurality of positions and, for each respective position in said plurality of positions, redefining the one or more substitutions for the respective position; and wherein

said redefining step (e) further comprises redefining said variant set to comprise one or more variants that are not in the subset of the antibody sequence space defined in ~~each having a substitution in a position in~~ said ~~redefined plurality of positions not present in any variant in the variant set selected by~~ said ~~initial selecting~~ step (b).

22. (Currently amended) The method of claim ~~21~~ 1 wherein

said modeling a sequence-activity relationship step (d) further comprises modeling a plurality of sequence-activity relationships, wherein each respective sequence-activity relationship in said plurality of sequence-activity relationships describes the relationship between (i) one or more substitutions at one or more positions of the antibody of interest represented by the variant set and (ii) the property measured for all or said portion of the variants in the variant set; and

said redefining said variant set (e) comprises redefining said variant set to comprise variants that include substitutions in said plurality of positions that are selected based on a combination function of said plurality of sequence-activity relationships.

23. (Currently amended) The method of claim 22, the method further comprising:

repeating said measuring step (c) based upon a property of all or a portion of the variants in said redefined variant set of step (e)~~, wherein a property of all or a portion of the variants in the redefined variant set is measured~~; and

weighting each respective sequence-activity relationship in said plurality of sequence activity relationships based on an agreement between (i) measured values for the property of variants in said redefined variant set and (ii) values for the property of variants in said redefined variant set that were predicted by said respective sequence-activity relationship, wherein

a first sequence-activity relationship that achieves better agreement between measured and predicted values than a second sequence-activity relationship receives a higher weight than said second sequence-activity relationship.

24-48. (Cancelled)

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49. (Currently amended) The method of claim 1 wherein

said measuring step (c) comprises synthesizing all or said portion of the variants in said variant set, and wherein

said property of a variant in said variant set is a level of expression of said variant in a host cell, a susceptibility of said variant to a post-translational modification, a killing of a pathogenic organism or a virus resulting from an activity of said variant, a modulation of a signaling pathway by said variant, a modulation of surface density of a cell-surface receptor by said variant, a binding of a cellular growth factor receptor by said variant, a binding of a receptor or a mediator of tumor-driven angiogenesis by said variant, a binding of a B cell surface antigen by said variant, a binding of a protein synthesized by said variant, an induction of an antibody-mediated cell killing by said variant, an induction of an antibody-dependent macrophage activity by said variant, an induction of a histamine release by said variant, an induction of or cross-reaction with an anti-idiotype antibody by said variant, an immunogenicity of said variant, a reduction of viral titer by said variant or an immunomodulatory activity of said variant.

50. (Currently amended) The method of claim 1, wherein said sequence-activity relationship has the form:

$$Y = f(w_1x_1, w_2x_2,\ldots, w_ix_i)$$

wherein,

Y is a quantitative measure of said property;

x_i is a descriptor of a substitution, a combination of substitutions, or a component of one or more substitutions, at one or more positions in said plurality of positions;

w_i is a weight applied to descriptor x_i; and

f( ) is a mathematical function.

51. (Currently amended) The method of claim 50, wherein said modeling comprises regressing:

$$Y = f(w_1x_1, w_2x_2,\ldots, w_ix_i).$$

52. (Currently amended) The method of claim 51, wherein regressing comprises linear regression, non-linear regression, logistic regressing, or partial least squares projection to latent variables.

53-65. (Cancelled)

66. (Currently amended) ~~The~~ A plurality of nucleic acid sequences comprising nucleotide sequences encoding all or a portion of the variants in the redefined variant set of ~~an instance of~~ step (e) [[e)]] of claim [[6]] 1.

67. (Currently amended) ~~A population of cells comprising nucleic acid sequences encoding a plurality~~ All or a portion of the variants in the redefined variant set of step (e) [[e)]] of claim 1.

68. (Currently amended) A population of cells comprising ~~the~~ a plurality of nucleic acid sequences, each nucleic acid sequence in the plurality of nucleic acid sequence encoding a ~~variants~~ variant in the redefined variant set of step (e) ~~e)~~ of claim 1.

69-73. (Cancelled)

74. (Currently amended) The method of claim 1 wherein said antibody of interest is from rat, mouse, chicken, cow, monkey, pig, dog, ~~or~~ rabbit, or human.

75. (Original) The method of claim 1 wherein said antibody of interest is a monoclonal antibody, a bispecific antibody, a multispecific antibody, a humanized antibody, a chimeric antibody, a camelised antibody, a single domain antibody, a single-chain Fvs (ScFv), a single chain antibody, a Fab fragment, a F(ab') fragment, a disulfide-linked Fvs (sdFv), or an anti-idiotypic (anti-Id) antibody.

76. (Original) The method of claim 1 wherein said antibody of interest is an epitope-binding fragment of a monoclonal antibody, an epitope-binding fragment of a bispecific antibody, an epitope-binding fragment of a multispecific antibody, an epitope-binding fragment of a humanized antibody, an epitope-binding fragment of a chimeric antibody, an epitope-binding fragment of a camelised antibody, an epitope-binding fragment of a single domain antibody, an

epitope-binding fragment of a single-chain Fvs (ScFv), an epitope-binding fragment of a single chain antibody, an epitope-binding fragment of a Fab fragment, an epitope-binding fragment of a F(ab') fragment, an epitope-binding fragment of a disulfide-linke Fvs (sdFv), or an epitope-binding fragment of an anti-idiotypic (anti-Id) antibody.

77. (Original) The method of claim 1 wherein said antibody of interest is an antibody fragment.

78. (Original) The method of claim 1 wherein a variant in the variant set comprises a monoclonal antibody, a bispecific antibody, a multispecific antibody, a humanized antibody, a chimeric antibody, a camelised antibody, a single domain antibody, a single-chain Fvs (ScFv), a single chain antibody, a Fab fragment, a F(ab') fragment, a disulfide-linked Fvs (sdFv), or an anti-idiotypic (anti-Id) antibody.

79. (Original) The method of claim 1 wherein a variant in the variant set comprises an epitope-binding fragment of a monoclonal antibody, an epitope-binding fragment of a bispecific antibody, an epitope-binding fragment of a multispecific antibody, an epitope-binding fragment of a humanized antibody, an epitope-binding fragment of a chimeric antibody, an epitope-binding fragment of a camelised antibody, an epitope-binding fragment of a single domain antibody, an epitope-binding fragment of a single-chain Fvs (ScFv), an epitope-binding fragment of a single chain antibody, an epitope-binding fragment of a Fab fragment, an epitope-binding fragment of a F(ab') fragment, an epitope-binding fragment of a disulfide-linke Fvs (sdFv), or an epitope-binding fragment of an anti-idiotypic (anti-Id) antibody.

80. (Original) The method of claim 1 wherein a variant in said variant set comprises an antibody fragment.

81. (Currently amended) The method of claim 1 wherein said measuring said property of all or said portion of the variants in the variant set of step (c) comprises:

    expressing a variant in the variant set in a cell line; and

    measuring a cell-surface receptor surface density of said cell line that includes said variant.

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82. (Currently amended) The method of claim 1 wherein said measuring said property of all or said portion of the variants in the variant set of step (c) comprises:

    expressing a variant in the variant set in a cell line; and

    measuring a cell surface receptor internalization rate of said cell line that includes said variant.

83. (Currently amended) The method of claim 1 wherein said measuring said property of all or said portion of the variants in the variant set of step (c) comprises:

    expressing a variant in the variant set in a cell line; and

    measuring a cell surface receptor post-translational modification of said cell line that includes said variant.

84. (Original) The method of claim 83 wherein said cell surface receptor post-translational modification is phosphorylation.

85. (Currently amended) The method of claim 1 wherein said measuring said property of all or said portion of the variants in the variant set of step (c) comprises:

    expressing a variant in said all or said portion of the variant set in a cell line; and

    measuring a binding of an antigen to said cell line that includes said variant.

86. (Original) The method of claim 85 wherein said antigen is a cellular growth factor receptor, a receptor of tumor-driven angiogenesis, a mediator of tumor-driven angiogenesis, a B cell surface antigen, or a protein synthesized by or in response to a pathogen.

87. (Currently amended) The method of claim 1 wherein said measuring said property of step (c) comprises measuring the ability for a variant in said variant set to immunospecifically bind to an antigen.

88. (Original) The method of claim 87 wherein said measuring comprises placing said variant in solution, spotting said variant onto a microchip, placing a polynucleotide encoding said variant in bacteria, placing a polynucleotide that codes for said variant in a spore, placing a

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polynucleotide that codes for said variant in a plasmid, or placing a polynucleotide that codes for said variant in phage.

89. (Currently amended) The method of claim 1 wherein said measuring said property <u>of step</u> <u>(c)</u> comprises assaying for a reduction of a viral titer <u>of a virus</u> in infected tissue culture cells by a variant in all or said portion of the variant set.

90. (Currently amended) [[the]] <u>The</u> method of claim 89<u>,</u> wherein the virus is hepatitis A virus, hepatitis B virus, hepatitis C virus, human papilloma virus, human immunodeficiency virus, respiratory syncitial virus, human adenovirus, fowl adenovirus 1, African swine fever virus, lymphocytic choriomeningitis virus, ippy virus, lassa virus, equine arteritis virus, human astrovirus 1, autographa californica nucleopolyhedrovirus, plodia interpunctella granulovirus, commelina yellow mottle virus, rice tungro bacilliform virus, mushroom bacilliform virus, infectious pancreatic necrosis virus, infectious bursal disease virus, drosophila x virus, alfalfa mosaic virus, tobacco streak virus, brome mosaic virus, cucumber mosaic virus, apple stem grooving virus, carnation latent virus, cauliflower mosaic virus, chicken anemia virus, beet yellows virus, cowpea mosaic virus, tobacco ringspot virus, avian infectious bronchitis virus, alteromonas phage pm2, pseudomonas phage phi6, hepatitis delta virus, carnation ringspot virus, red clover necrotic mosaic virus, sweet clover necrotic mosaic virus, pea enation mosaic virus, ebola virus zair, soil-borne wheat mosaic virus, beet necrotic yellow vein virus, sulfobolus virus 1, maize streak virus, beet curly top virus, bean golden mosaic virus , duck hepatitis B virus, human herpesvirus, human herpesvirus, ateline herpesvirus 2, barley stripe mosaic virus, cryphonectria hypovirus 1-ep713,raspberry bushy dwarf virus, acholeplasma phage 151, chilo iridescent virus, goldfish virus 1, enterobacteria phage ms2, enterobacteria phage qbeta, thermoproteus virus 1, maize chlorotic mottle virus, maize rayado fino virus, coliphage phix174, spiromicrovirus, spiroplasma phage, bdellomicrovirus, bdellovibrio phage, chlamydiamicrovirus, chlamydia phage 1, coliphage t4, tobacco necrosis virus, nodamura virus, influenzavirus a, influenzavirus C, thogoto virus, rabbit (shope) papillomavirus, human parainfluenza virus, measles virus, rubulavirus, mumps virus, human respiratory syncytial virus, gaeumannomyces graminis virus, penicillium chrysogenum virus, white clover cryptic virus, white clover cryptic virus 2, minute mice virus, adeno-associated virus, junonia coenia densovirus, bombyx mori virus, aedes aegypti densovirus, 1-paramecium bursaria chlorella nc64a virus, paramecium bursaria chlorella virus, 2-paramecium bursaria chlorella pbi virus,

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3-hydra viridis chlorella virus, human poliovirus 1, human rhinovirus 1A, hepatovirus, encephalomyocarditis virus, foot-and-mouth disease virus, acholeplasma phage l2, coliphage t7, campoletis sonorensis virus, cotesia melanoscela virus, potato virus X, potato virus Y, ryegrass mosaic virus, barley yellow mosaic virus, fowlpox virus, sheep pox virus, swinepox virus, molluscum contagiosum virus, yaba monkey tumor virus, entomopoxvirus A, melolontha melolontha entomopoxvirus, amsacta moorei entomopoxvirus, chironomus luridus entomopoxvirus, reovirus 3, epizootic hemarrhogic disease virus 1, or simian rotavirus SA11.

91. (Currently amended) The method of claim 1 wherein said measuring said property <u>of step (c)</u> comprises assaying for a reduction of a viral titer <u>of a virus</u> in an animal model by a variant in all or said portion of the variant set.

92. (Currently amended) The method of claim 91 wherein the virus [[is]] is hepatitis A virus, hepatitis B virus, hepatitis C virus, human papilloma virus, human immunodeficiency virus, respiratory syncitial virus, human adenovirus, fowl adenovirus 1, African swine fever virus, lymphocytic choriomeningitis virus, ippy virus, lassa virus, equine arteritis virus, human astrovirus 1, autographa californica nucleopolyhedrovirus, plodia interpunctella granulovirus, commelina yellow mottle virus, rice tungro bacilliform virus, mushroom bacilliform virus, infectious pancreatic necrosis virus, infectious bursal disease virus, drosophila x virus, alfalfa mosaic virus, tobacco streak virus, brome mosaic virus, cucumber mosaic virus, apple stem grooving virus, carnation latent virus, cauliflower mosaic virus, chicken anemia virus, beet yellows virus, cowpea mosaic virus, tobacco ringspot virus, avian infectious bronchitis virus, alteromonas phage pm2, pseudomonas phage phi6, hepatitis delta virus, carnation ringspot virus, red clover necrotic mosaic virus, sweet clover necrotic mosaic virus, pea enation mosaic virus, ebola virus zair, soil-borne wheat mosaic virus, beet necrotic yellow vein virus, sulfobolus virus 1, maize streak virus, beet curly top virus, bean golden mosaic virus , duck hepatitis B virus, human herpesvirus, human herpesvirus, ateline herpesvirus 2, barley stripe mosaic virus, cryphonectria hypovirus 1-ep713,raspberry bushy dwarf virus, acholeplasma phage 151, chilo iridescent virus, goldfish virus 1, enterobacteria phage ms2, enterobacteria phage qbeta, thermoproteus virus 1, maize chlorotic mottle virus, maize rayado fino virus, coliphage phix174, spiromicrovirus, spiroplasma phage, bdellomicrovirus, bdellovibrio phage, chlamydiamicrovirus, chlamydia phage 1, coliphage t4, tobacco necrosis virus, nodamura virus, influenzavirus a, influenzavirus C, thogoto virus, rabbit (shope) papillomavirus, human

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parainfluenza virus, measles virus, rubulavirus, mumps virus, human respiratory syncytial virus, gaeumannomyces graminis virus, penicillium chrysogenum virus, white clover cryptic virus, white clover cryptic virus 2, minute mice virus, adeno-associated virus, junonia coenia densovirus, bombyx mori virus, aedes aegypti densovirus, 1-paramecium bursaria chlorella nc64a virus, paramecium bursaria chlorella virus, 2-paramecium bursaria chlorella pbi virus, 3-hydra viridis chlorella virus, human poliovirus 1, human rhinovirus 1A, hepatovirus, encephalomyocarditis virus, foot-and-mouth disease virus, acholeplasma phage 12, coliphage t7, campoletis sonorensis virus, cotesia melanoscela virus, potato virus X, potato virus Y, ryegrass mosaic virus, barley yellow mosaic virus, fowlpox virus, sheep pox virus, swinepox virus, molluscum contagiosum virus, yaba monkey tumor virus, entomopoxvirus A, melolontha melolontha entomopoxvirus, amsacta moorei entomopoxvirus, chironomus luridus entomopoxvirus, reovirus 3, epizootic hemarrhogic disease virus 1, or simian rotavirus SA11.

93. (Original) The method of claim 1 wherein said measuring said property of step (c) comprises assaying for a change in rate of proliferation of cells grown in a culture by a variant in all or said portion of the variant set.

94. (Currently amended) The method of 93 wherein the culture cells grown in the culture are [[is]] tumor cells, a cell line derived from tumor cells, a cell line derived from breast cancer cells, a cell line derived from ovarian cancer cells, a cell line derived from lung cancer cells, a cell line derived from bone cancer cells, a cell line derived from fibroblast cancer cells, a cell line derived from hematopoetic cancer cells, a cell line derived from testicular cancer cells, a cell line derived from colon cancer cells, a cell line derived from prostate cancer cells, or a cell line derived from leukemia cells.

95. (Currently amended) The method of claim 1 wherein said measuring said property of step (f) comprises assaying for a change in rate of proliferation of a specific cell type in an animal model by a variant in all or said portion of the redefined variant set.

96. (Original) The method of 95 wherein the specific cell type is a tumor cell type.

97. (Currently amended) The method of claim [[96]] 95 wherein the specific cell type is derived from a breast cancer tumor, an ovarian cancer tumor, a lung cancer tumor, a bone

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cancer tumor, a fibroblast cancer, a hematopoetic cancer, a testicular cancer, a colon cancer, a prostate cancer, or a leukemia.

98. (Currently amended) A method of preventing, treating or ameliorating one or more symptoms associated with a condition in a subject that is caused by a pathogenic organism, said method comprising administering a prophylactically or therapeutically effective amount of a ~~the~~ variant in the redefined variant set of claim ~~2~~ 1.

99. (Currently amended) A method of preventing, treating or ameliorating one or more symptoms associated with a condition in a subject that is caused by a virus, said method comprising administering a prophylactically or therapeutically effective amount of ~~the~~ a variant in the redefined variant set of claim ~~2~~ 1.

100. (Currently amended) A method of preventing, treating or ameliorating one or more symptoms associated with a condition in a subject that is caused by a cancer, said method comprising administering a prophylactically or therapeutically effective amount of ~~the~~ a variant in the redefined variant set of claim ~~2~~ 1.

101-120. (Cancelled)

121. (New) The method of claim 1, wherein a second value in the plurality of second values is a standard deviation of a corresponding first value in the plurality of first values.

122. (New) The method of claim 1, wherein each variant in the redefined variant set of step (e) differs by fewer than 5 substitutions from at least one variant for which the property has been measured in step (c).

123. (New) The method of claim 1 wherein said redefining of said variant set further comprises:

computing a modified first score in the plurality of first scores by modifying the first score based on a function of the second score, in the plurality of second scores, that corresponds to the first score, thereby computing a plurality of modified first scores; and

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wherein said function of said plurality of first values and said plurality of second values comprises using the modified first score for each of the one or more substitutions at the plurality of positions as a basis for including or excluding substitutions from the redefined variant set.

124. (New) The method of claim 5, wherein

the contribution of each respective rule in the plurality of rules to the defining of said antibody sequence space is independently weighted by a rule weight in a plurality of rule weights corresponding to the respective rule; and

the plurality of rule weights are calculated based on a comparison, for a plurality of substitutions in the variant set of (i) a value assigned to the respective substitution by the sequence-activity relationship, and (ii) a score assigned by the plurality of rules to the respective substitution.

125. (New) The method of claim 1, wherein said modeling a sequence activity relationship step (d) comprises deriving a relationship between (i) a physico-chemical property of one or more substitutions at one or more positions of the antibody of interest represented by the variant set and (ii) the property measured for all or the portion of the variants in the variant set.

126. (New) The method of any one of claims 1-6, 8-14, 16, 20-23, 49-52, 66-68, 74-100, or 121-125 implemented on a computer.

127. (New) A computer program product encoding instructions for implementing the method according to any one of claims 1-6, 8-14, 16, 20-23, 49-52, 66-68, 74-100, or 121-125.